

PATENT  
0825-0176P

## IN THE U.S. PATENT AND TRADEMARK OFFICE

APPLICANT: BOREN, Thomas et al. CONF: 3104  
SERIAL NO.: 10/761,201 GROUP: 1645  
FILED: January 22, 2004 EXAMINER: PORTNER, V.  
FOR: HELICOBACTER PYLORI ADHESIN BINDING GROUP ANTIGEN

**DECLARATION SUBMITTED UNDER 37 C.F.R. § 1.132**

Honorable Commissioner  
Of Patents and Trademarks  
P.O. Box 1450  
Alexandria, VA 22313-1450

July 28th, 2006

Sir:

I, professor Lennart Hammarström of the Karolinska Institutet, Stockholm,  
Sweden, do hereby declare the following:

I have attached a copy of my curriculum vitae to this Declaration.

I am a professor of clinical immunology and have worked in this field for 30  
years.

I am familiar with the above referenced patent application, as well as the  
development, usages and properties of the BabA adhesion protein and Lewis B  
antigens and antibodies.

I have read and understand the subject matter of the Office Action of March 3,  
2006.

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The following comments are offered in support of the patentability of the instant invention.

The Examiner states that the Durrant et al. reference destroys the novelty of the 10/761,201 application and seems to use the Essery et al. reference to support her position. That is, the Examiner says that Essery et al. show that an anti-idiotypic antibody that recognizes the Lewis B antigen structure would bind to the BabA protein (which itself binds to the Lewis B antigen). I disagree.

The antibodies against Lewis A and Lewis B recognize unique antigens and their specificity is due to sequence differences in the hypervariable region. Thus, by definition, the anti-idiotypic antisera raised by Essery et al. are not directed against the antigen binding site, but rather a paratope which is shared, to some degree, by the tested monoclonals (anti- Lewis<sup>a</sup> and anti- Lewis<sup>b</sup>). The reference claims that this paratope is not shared with 4 other monoclonal antibodies, but there is no data provided to support this claim (see Essery et al., page 19 "Specificity of the proteins A sepharose reagent"). In fact, Essery et al. states "the paratope of the Fab portion of the anti-idiotypic antibody appears to have a structure similar to the Lewis<sup>a</sup> antigen" (emphasis added). That is, the reference does not say *identical* to the Lewis<sup>a</sup> antigen.

If one does believe that there is indeed specific binding of the anti-idiotypic antiserum of Essery et al. to BabA, it follows that this antigen is also present on other bacteria, such as *N. gonorrhoeae*, and fungi such as *C. albicans*, as one of the two tested *N. gonorrhoeae* strains was recognized by the anti-idiotypic antiserum (see page 19,

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column 2, last paragraph, lines 5-7) as did one of two *C. ablicans* strains (see page 20, column 1, first paragraph, lines 5-8). However, these microorganisms do not express BabA, therefore the anti-idiotypic antiserum described by Essery et al must recognize another protein or structure.

The Examiner also notes that the claims do not recite that the specific binding is carried out by the hypervariable region. Stating this fact is superfluous. Researchers working with antibodies understand that specific binding is carried out by the antigen binding site of the specific antibody, as determined by the sequence of the hypervariable region. If binding to a sugar moiety on the antibodies would confer specific binding, there would be no need for immunization in order to raise anti-BabA-specific antibodies.

Lastly, the Examiner seems to believe that it would be obvious to modify the Boren composition to obtain the antibodies claimed in the application and then to make a kit. Again, I disagree.

The Boren 1995 paper describes a finding that is the opposite of the invention in application 10/761,201, which claims an antibody preparation that is dependent on the antigen specific binding properties of the antibody itself. That is, normal antibodies that demonstrates binding properties due to the variable domains of the antibody. In contrast, the 1995 Boren paper describes the ability of the *H. pylori* adhesion protein (BabA) to bind to Lewis b antigens present on glycosylated proteins (an IgA antibody preparation) in human milk. The paper also describes a similar IgA antibody preparation


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purified from human sera, which are the IgA antibodies that are present in human blood. These antibodies are low in glycosylation and do not present Lewis b antigens and thus, they do not inhibit bacterial binding because the *H. pylori* Lewis b binding adhesion protein (BabA) does not bind to non-glycosylated antibodies.

To summarize, in my opinion the Examiner is incorrect in her assertions that the 10/761,201 application is not novel and is obvious.

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The undersigned hereby declares that all statements made herein based upon knowledge are true, and that all statements made based upon information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

DATED: July 28<sup>th</sup>, 2006

Professor Lennart Hammarström

**CV****Name**

Lennart Hammarström, born December 31st, 1950

**Nationality**

Swedish

**Education**

Doctoral exam 1975 (Karolinska Institutet)  
Thesis 1979 (molecular basis of B lymphocyte activation)(Karolinska Institutet)  
Docent (lecturer) in Immunology 1979 (Karolinska Institutet)  
Specialist in Clinical Immunology 1984 (Huddinge Hospital)  
Associate Professor in Clinical Immunology 1985 (Huddinge Hospital)  
Professor (biträdande Professor) 1997 (Karolinska Institutet)  
Professor 1999 (Karolinska Institutet)  
Professor (guest professor) 1999 (Beijing Medical University)

**Position**

Research career award from the Swedish Medical Research Council (autoimmunity and inflammation) at the Karolinska Institutet (1991 - 1997)  
Head of the Clinical Immunology Laboratory at Huddinge Hospital (1997 - 2001)  
Head of the division of Clinical Immunology within the department of Laboratory Medicine (Karolinska Institutet) at Huddinge Hospital (2001 -)  
Lecturer in basic and clinical immunology for medical and dental students at the Karolinska Institutet (1975 - 2005) and responsible for the course in clinical immunology for medical students and for the course in immunology for dental students at Huddinge hospital  
Tutor for 15 students who have passed their Ph. D. thesis and training 6 additional PhD students

**Scientific interest**

Immunodeficiency, immunogenetics, regulation of antibody production, immunotherapy.  
Published more than 400 scientific articles in these fields

**Administration**

Member of the Adverse Drug Reaction Committee of the Swedish National Board for Health and Welfare (FDA) (1988 - 1995)  
President of the Swedish Society for Immunology (1991 - 1997)  
Member of the Biotechnology committee of the Swedish Pharmaceutical Association (1994 - 1996)  
Member of the steering committee of ESID (European Society for Immunodeficiency) (1994 - 2002)  
Member of the Swedish Medical Research Council advisory board (1995 - 2001)  
Member of the WHO/IUIS committee on Primary Immunodeficiencies (1996 - 2003)  
Member of the Editorial Board of J of Clinical Immunology (1996 - 2000)  
Member of the IUIS committee on Veterinary Immunoglobulins (1997 - 2002)  
Member of the EAACI committee on Immunology (1998 - 2000)  
Member of the board of SSF (Swedish Foundation for Strategic Research) (Biocompatible materials) (1999 - 2004)  
Member of the board of CFA (Center for allergy research at the Karolinska Institute (2002 - 2003)  
Member of the research education committee (forskarutbildningsstyrelsen) at the Karolinska Institutet (2002 - 2005)